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Rate and Product Studies with Benzyl and *p*-Nitrobenzyl Chloroformates under Solvolytic Conditions[†]

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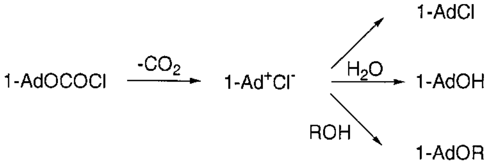
The specific rates of solvolysis of *p*-nitrobenzyl chloroformate are well correlated using the extended Grunwald−Winstein equation, with a high sensitivity (l) to changes in solvent nucleophilicity (N_T) and a moderate sensitivity (m) to changes in solvent ionizing power (Y_{Cl}). The values are consistent with a rate-determining association within an association−dissociation pathway. The selectivity values (S) for the attack at the acyl carbon show a modest preference for ethanol over water and a relatively high preference for ethanol over 2,2,2-trifluoroethanol (TFE). The solvolyses of benzyl chloroformate show similar characteristics in solvents of relatively high nucleophilicity and/or low ionizing power. In solvents with considerable fluoro alcohol content, an ionization mechanism, accompanied by loss of carbon dioxide, leads to benzyl chloride, benzyl alcohol, and benzyl alkyl ether. A new correlation now applies, with a much lower l value and somewhat higher m value. The S values for this pathway are close to unity, even in TFE−ethanol mixtures, consistent with the components of the binary solvent capturing a highly reactive carbocation.

Phenyl chloroformate (PhOCOCl) is well established as undergoing solvolysis over a wide range of hydroxylic solvents by an addition−elimination mechanism, with the addition step being rate-determining.[1] The mechanism can be switched to one involving ionization by replacement of oxygen by sulfur[2,3] and phenyl chlorodithioformate (PhSCSCl) reacted exclusively by an ionization pathway.[3] Methyl[4] and ethyl[5] chloroformates favor an addition−elimination pathway,[6] although there is evidence for the solvolyses having an ionization component in highly ionizing and weakly nucleophilic solvents.

The tertiary 1-adamantyl chloroformate (1-AdOCOCl) reacts almost exclusively by an ionization pathway which, unlike that for phenyl chlorodithioformate,[3] also includes loss of carbon dioxide to give the relatively stable 1-adamantyl cation. This cation can then unite with the chloride counterion, resulting in an overall decomposition pathway; it can react with the water component of a solvent to give 1-adamantanol; or it can react with an alcohol component to give the ether (Scheme 1). Of the alcohol-containing solvents included in the study,[7] only in pure ethanol was a trace of the mixed carbonate (1-AdOCO$_2$Et) observed.

Scheme 1



It is well-known, especially to one of the authors,[6] that benzyl chloroformate (**1**) slowly builds up pressure on standing at room temperature, and this can lead to glass containers fracturing with explosive violence. This suggests that **1** may also be capable of undergoing decomposition in competition with solvolysis. Further support for this belief comes from the observation of accompanying decomposition, with loss of N$_2$O, when benzyl azoxytosylate is subjected to solvolytic conditions[8] and from the loss of N$_2$ during reactions of *N*-benzyl-*N*-nitrosoamides in various solvents.[9] The solvolytic behavior of **1** and its ring-substituted derivatives is of especial interest since, for many years, they have been recommended reagents for the introduction of a protecting group during peptide syntheses.[10]

The effect of incorporating a *p*-nitro substituent, to give *p*-nitrobenzyl chloroformate (**2**), is also included in the

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[†] This paper is dedicated to Professor Rolf Huisgen on the occasion of his 80th birthday and in recognition of his many contributions to organic chemistry.

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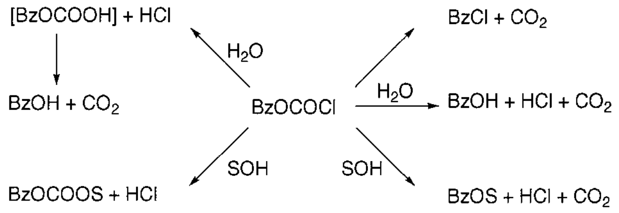
Scheme 2



study. This substitution will decelerate reactions involving ionization and accelerate the competing addition−elimination pathway, especially when the addition step is rate-determining.

A kinetic investigation involving the determination of infinity titers could also give an indication as to whether decomposition to benzyl chloride is accompanying the solvolysis (Scheme 2). All of the solvolytic pathways produce HCl and, if a stable infinity titer is obtained which is less than the theoretical value, the difference could be assumed to correspond to benzyl chloride formation (benzyl chloride undergoes solvolysis only very slowly under the conditions used to study the reactions of **1**[11]). However, the specific rates of reaction, based on the experimental infinity titer, will be those for the overall reaction, solvolysis plus decomposition.

Product studies, conveniently and comprehensively carried out by gas chromatography or gas chromatography−mass spectrometry, will directly show the presence or absence of benzyl or *p*-nitrobenzyl chloride and will determine the extent to which formation of other products involves loss of CO_2. For reaction with the alcohol component of a solvent, the interpretation will be unambiguous, with formation of either ether or ester. For reaction with a water component, the half ester can now be formed (with carbon dioxide retained), and this rapidly loses CO_2 at this stage,[12] providing a second route to the alcohol, in addition to the route involving capture of the benzyl cation by water. The relative importance of the two pathways for alcohol formation could be directly assessed by use of an ^{18}O label in either substrate or solvent, but this was not considered to be necessary in the context of the present study.

Results

Table 1. Specific Rates of Solvolysis of Benzyl Chloroformate (1) and *p*-Nitrobenzyl Chloroformate (2) in Several Solvents at 25.0 °C, Accompanied by Solvent Nucleophilicity (N_T) and Ionizing Power (Y_{Cl}) Values

solvent[a]	$10^5 k$ (**1**), s^{-1} [b]	$10^5 k$ (**2**), s^{-1} [b]	N_T[c]	Y_{Cl}[d]
100% EtOH	5.16 ± 0.14[e]	18.6 ± 0.1	0.37	−2.52
90% EtOH	12.9 ± 0.2	55.4 ± 0.3	0.16	−0.94
80% EtOH	17.7 ± 0.2	74.7 ± 0.3	0.00	0.00
70% EtOH	21.5 ± 0.4	88.6 ± 0.6	−0.20	0.78
60% EtOH	25.6 ± 0.6	106 ± 4	−0.38	1.38
50% EtOH	31.9 ± 0.9	114 ± 2	−0.58	2.02
100% MeOH	18.8 ± 0.2	62.4 ± 0.3[f]	0.17	−1.17
90% MeOH	38.4 ± 0.5	132 ± 1	−0.01	−0.18
80% MeOH	55.4 ± 0.4	187 ± 2	−0.06	0.67
95% acetone		0.874 ± 0.010	−0.49	−3.19
90% acetone		2.92 ± 0.02	−0.35	−2.22
80% acetone	2.13 ± 0.05	9.07 ± 0.06	−0.37	−0.80
70% acetone	4.23 ± 0.07	17.2 ± 0.1	−0.42	0.17
60% acetone	7.62 ± 0.17		−0.52	1.00
90% dioxane		4.77 ± 0.03		
80% dioxane	4.54 ± 0.09	13.5 ± 0.1	−0.46	
100% TFE[g]	1.78 ± 0.05		−3.93	2.81
97% TFE[g]	1.93 ± 0.06		−3.30	2.83
90% TFE[g]	2.37 ± 0.08	0.191 ± 0.010	−2.55	2.83
80% TFE[g]	3.44 ± 0.08	0.792 ± 0.020	−2.19	2.90[h]
70% TFE[g]	4.82 ± 0.06		−1.98	2.96
50% TFE[g]	9.39 ± 0.15		−1.73	3.16
97% HFIP[g]	13.8 ± 0.5		−5.26	5.08
90% HFIP[g]	11.5 ± 0.3		−3.84	4.31
70% HFIP[g]	11.3 ± 0.7		−2.94	3.83
90T−10E[i]	1.08 ± 0.02		−2.62[h]	2.32[h]
80T−20E[i]	0.692 ± 0.047	0.362 ± 0.012	−1.76	1.89
60T−40E[i]	0.993 ± 0.041	2.16 ± 0.04	−0.94	0.63
40T−60E[i]	2.19 ± 0.05	6.79 ± 0.05	−0.34	−0.48
20T−80E[i]	3.90 ± 0.04	14.0 ± 0.2	0.08	−1.42

[a] Unless otherwise indicated, on a v/v basis, at 25.0 °C, with the other component water; substrate concentration of 0.0056 mol dm^{-3}. [b] With associated standard deviations. [c] From ref 13. [d] From refs 15 and 16. [e] In the presence of 0.0200, 0.0300, 0.0400, and 0.0500 mol dm^{-3} NEt_4Cl, values of 5.31 ± 0.08, 5.41 ± 0.08, 5.52 ± 0.05, and 5.65 ± 0.07, respectively, were obtained. [f] Value in CH_3OD of 25.8 ± 0.3, and solvent deuterium isotope effect (k_{MeOH}/k_{MeOD}) of 2.42 ± 0.03. [g] On a w/w basis. [h] Interpolated value. [i] T-E are 2,2,2-trifluoroethanol−ethanol mixtures.

The specific rates of solvolysis (or solvolysis plus decomposition) for **1** and *p*-nitrobenzyl chloroformate (**2**), at 25.0 °C, are reported in Table 1. The solvents consisted of ethanol, methanol, 2,2,2-trifluoroethanol (TFE), 90−50% aqueous ethanol, 90% and 80% aqueous methanol, 95%−60% aqueous acetone, 90% and 80% aqueous dioxane, 97%−50% aqueous TFE, and the full range of TFE−ethanol mixtures. A total of 27 solvents was studied for reactions of **1**, including also three mixtures of water and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), and 21 solvents for reaction of **2**. Also included in Table 1 are the Grunwald−Winstein N_T[13,14] and Y_{Cl}[15,16] values, as abstracted from the literature. Since Y_{Cl} values are not available for the two aqueous dioxane solvents, the Grunwald−Winstein treatments of the data use only 26 solvents for **1** and only 19 solvents for **2**. A few runs were carried out using a considerably older, unpurified sample of **1**, indicated by ^1H NMR to contain 40% benzyl chloride. The specific rates obtained with this sample were essentially identical to those obtained using a highly purified sample.

For ethanol, 80% ethanol, methanol, and 2-propanol, runs were also carried out at three additional temperatures for both **1** and **2**, and these data are reported in Table 2 together with data for the solvolysis of **2** in 90% dioxane at two additional temperatures. These values, together with those for these solvents at 25.0 °C (Table 1), were used to obtain the enthalpies and entropies of activation reported in Table 3.

For reactions of **1** in ethanol, TFE, 90−50% aqueous ethanol, 97−50% aqueous TFE, and the full range of TFE−ethanol mixtures (a total of 17 solvents), product studies were carried out using gas chromatography with

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Table 2. Specific Rates of Solvolysis of Benzyl Chloroformate (1) and *p*-Nitrobenzyl Chloroformate (2) at Various Temperatures

solvent[a]	T, °C	$10^5\,k$ (**1**), s^{-1} [b]	$10^5\,k$ (**2**), s^{-1} [b]
100% EtOH	20.0		12.4 ± 0.1
	30.0	7.78 ± 0.13[c,d]	27.6 ± 0.2
	35.0	11.6 ± 0.2	40.6 ± 0.6
	41.0	19.4 ± 0.4[e]	
100% MeOH	20.0		42.4 ± 0.5
	30.0	27.4 ± 0.4	87.5 ± 1.5
	35.0	43.2 ± 0.6	122 ± 3
	40.0	61.7 ± 0.9	
80% EtOH	15.0		36.5 ± 0.3
	20.0		53.5 ± 1.6
	30.0	25.9 ± 0.4	107 ± 2
	35.0	38.0 ± 0.6	
	41.0	60.3 ± 1.1	
100% *i*-PrOH	40.0		6.38 ± 0.05
	45.0		9.28 ± 0.06
	50.0	4.44 ± 0.10	13.4 ± 0.1
	55.0	6.54 ± 0.23	
	60.0	9.12 ± 0.18	
90% dioxane	30.0		6.83 ± 0.30
	35.0		9.62 ± 0.42

[a,b] See Table 1. [c] At 30.2 °C. [d] Reference 21 reports a specific rate of 12 (±1) × 10^{-5} s^{-1} at 29.6 °C. [e] Reference 21 reports a specific rate of 29 (±3) × 10^{-5} s^{-1}.

Table 3. Enthalpies and Entropies of Activation for Solvolyses of Benzyl Chloroformate (1) and *p*-Nitrobenzyl Chloroformate (2)[a]

compound	solvent[b]	$\Delta H_{298}^{\ddagger}$, kcal mol^{-1} [c]	$\Delta S_{298}^{\ddagger}$, eu[c,d]
1	100% EtOH[e]	14.8 ± 0.3	−28.4 ± 1.2
	100% MeOH	14.3 ± 0.5	−27.5 ± 1.7
	80% EtOH	13.7 ± 0.1	−29.8 ± 0.4
	100% *i*-PrOH[f,g,h]	14.8 ± 0.5	−32.8 ± 1.7
2	100% EtOH	13.5 ± 0.1	−30.2 ± 0.4
	100% MeOH	12.0 ± 0.2	−33.1 ± 0.6
	80% EtOH	11.6 ± 0.1	−33.8 ± 0.4
	100% *i*-PrOH[f,h,i]	14.3 ± 0.1	−32.1 ± 0.2
	90% dioxane	12.2 ± 0.1	−37.3 ± 0.5

[a] Specific rates from Tables 1 and 2. [b] Using data at four temperatures unless otherwise specified. [c] With associated standard error. [d] cal mol^{-1} K^{-1}. [e] Reference 21 reports values, for a temperature range of 21−48 °C, of 14.3 kcal mol^{-1} for $\Delta H^{\ddagger}$ and −34.2 eu for $\Delta S^{\ddagger}$. [f] Using data at three temperatures. [g] Extrapolated specific rate at 25.0 °C of 0.60 (±0.05) × 10^{-5} s^{-1}. [h] Values at 323 K. [i] Extrapolated specific rate at 25.0 °C of 1.91 (± 0.02) × 10^{-5} s^{-1}.

response-calibrated flame ionization detection, and those results are reported in Table 4. Since the reaction pattern for **2** was less complicated, product studies were carried out in only six solvents (ethanol, 80% and 60% ethanol, 80% TFE, and two TFE−ethanol mixtures), with the analyses employing gas chromatography−mass spectroscopy; these results are reported in Table 5.

Discussion

Solvolysis of *p*-Nitrobenzyl Chloroformate (2). In the presence of the *p*-nitro group the ionization mechanism is disfavored, and the addition step within an addition−elimination mechanism is favored. The bias is sufficient for the addition−elimination mechanism to be observed over the full range of solvents, in contrast to the more complicated reaction pattern observed for the parent compound **1**. A similar situation was observed in studies of the solvolyses of benzoyl chlorides, where the parent showed a duality of mechanism,[17] but introduction of a *p*-nitro substituent led to an addition−elimination pathway over the full range of the studied solvents.[18]

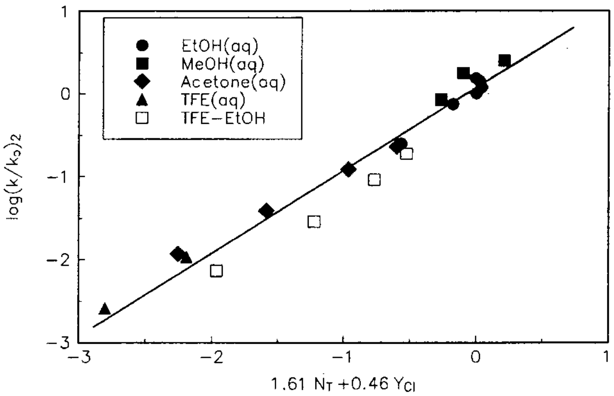

Figure 1. Plot of log(k/k_0) for solvolyses of *p*-nitrobenzyl chloroformate against (1.61 N_T + 0.46 Y_{Cl}).

Application of the extended Grunwald−Winstein equation (eq 1) to the specific rates of solvolysis of **2** (from Table 1) leads to a good correlation against N_T and Y_{Cl} (correlation coefficient of 0.9754 and *F*-test value of 157

$$\log(k/k_0) = lN_T + mY_X + c \qquad (1)$$

for 19 solvents) with values of 1.61 ± 0.09 for *l*, 0.46 ± 0.04 for *m*, and 0.04 ± 0.22 for *c*. The relationship is presented graphically in Figure 1. In eq 1, k and k_0 are the specific rates of solvolysis in a given solvent and in the standard solvent (80% ethanol), respectively; *l* is the sensitivity toward changes in solvent nucleophilicity (N_T);[13,14] *m* is the sensitivity toward changes in ionizing power (Y_X for a leaving group X);[15] *c* is a residual (constant) term. The reported values for *l* and *m* are typical of those for a rate-determining addition within an addition−elimination pathway for nucleophilic substitution at a carbonyl carbon. For example, the solvolyses of phenyl chloroformate are well established[1] as proceeding by an addition−elimination pathway, and the corresponding values are 1.68 ± 0.10 for *l* and 0.57 ± 0.06 for *m*. Similarly, methyl chloroformate has values of 1.59 ± 0.09 for *l* and 0.58 ± 0.05 for *m*.[4]

Activation parameter values for solvolyses of **2** in five solvents are tabulated in Table 3. The entropies of activation, in the range of −30 to −37 cal mol^{-1} K^{-1}, are consistent with the bimolecular nature of the proposed rate-determining step.

The product studies for the solvolyses of **2** (Table 5) are also consistent with an addition−elimination pathway. All of the products can be rationalized in terms of mixed carbonate esters being formed from reaction with either a pure alcohol or with the alcohol component of a mixed solvent and *p*-nitrobenzyl alcohol being formed after carbon dioxide loss from an initially formed hydrogen carbonate (Scheme 3). In particular, there was no evidence for *p*-nitrobenzyl chloride, from a competing decomposition,[7] or for the appropriate mixed ether, which

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Table 4. Percentages of Products Formed in the Solvolysis−Decomposition Reactions of Benzyl Chloroformate (BzOCOCl, 1) in Various Hydroxylic Solvents at 25.0 °C

solvent[a]	BzOTfe[b]	BzOEt	BzCl	$BzOCO_2Tfe$[b]	BzOH	$BzOCO_2Et$
100% EtOH		0.58	1.29[c]			98.12
90% EtOH		0.64	1.60		14.86	82.92
80% EtOH		0.91	1.64		22.21	75.25
70% EtOH		1.17	1.79		28.67	68.38
60% EtOH		1.51	2.06		35.06	61.14
50% EtOH		1.90	2.29		41.98	53.84
100% TFE	52.10		47.90		trace[d]	
97% TFE	46.68		45.72		7.60	
90% TFE	38.51		36.87	0.16	24.46	
80% TFE	29.03		28.06	0.33	42.58	
70% TFE	21.52		21.09	0.52	56.87	
50% TFE	11.81		11.96	0.61	75.61	
90T−10E	45.59	7.83	44.53	trace[d]	0.21	1.85
80T−20E	34.73	13.00	37.30	0.17	trace[d]	14.81
60T−40E	6.72	7.67	13.99	0.56	0.41	70.64
40T−60E	0.68	3.92	13.68	0.31	0.44	80.97
20T−80E	trace[d]	2.87	11.21	trace[d]	0.53	85.39

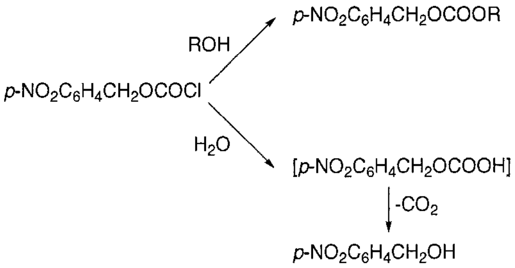
[a] Ethanol−H_2O and TFE−ethanol mixtures (T-E) are on a v/v basis; TFE−H_2O mixtures are on a w/w basis. [b] Tfe represents the 2,2,2-trifluoroethyl group. [c] In the presence of 0.0200 and 0.0500 mol dm^{-3} NEt_4Cl, the value increases to 3.4% and 6.9%, respectively. [d] Less than 0.1%.

Table 5. Percentages of Products Formed in the Solvolyses of *p*-Nitrobenzyl Chloroformate (*p*-$NO_2BzOCOCl$, 2) in Various Hydroxylic Solvents at 25.0 °C

solvent[a]	*p*-NO_2BzOCO_2Tfe[b]	*p*-NO_2BzOH	*p*-NO_2BzOCO_2Et
100% EtOH		trace	100.0
80% EtOH[c]		16.5	83.5
60% EtOH[d]		26.0	74.0
80% TFE[e]	10.2	89.8	
80T−20E[f]	1.1		98.9
60T−40E	trace		100

[a,b] See footnotes to Table 4. [c] *S* value (see eq 2) of 4.1. [d] *S* value (see eq 2) of 6.1. [e] *S* value (see eq 2) of 0.16. [f] *S* value (reaction with TFE relative to reaction with ethanol) of 0.0035.

Scheme 3



would have been formed by an ionization pathway involving loss of CO_2, followed by reaction of the carbocation with an alcohol component of the solvent.

The selectivity (*S*) values are presented (Table 5), for solvolysis in an aqueous alcohol, as the rate of product formation from interaction with an alcohol molecule relative to the rate of product formation from interaction with a water molecule. In this way, *S* is expressed[19] as in eq 2. In 80% and 60% ethanol, the values for *S* are 4.1

$$\text{selectivity } (S) = ([\text{ester}]_{\text{products}} \times [\text{water}]_{\text{solvent}}) / ([\text{acid}]_{\text{products}} \times [\text{alcohol}]_{\text{solvent}}) \quad (2)$$

and 6.1, respectively. These values are slightly higher but similar to those which have been observed for other solvolyses of carbonyl chlorides believed to follow the addition−elimination pathway. Corresponding values of 2.0 and 3.1 have been observed for *p*-nitrobenzoyl chloride,[18a] of 2.6 and 3.7 for *p*-chlorobenzoyl chloride,[17b] and of 2.6 and 4.2 for *p*-nitrophenyl chloroformate.[20]

For reaction in 80% aqueous TFE (w/w), we observe an *S* value of 0.16, corresponding to reaction with any given water molecule being 6.3 times more likely than with any given TFE molecule. For reaction in 80% TFE−20% ethanol (v/v) only a very small amount of reaction with TFE is observed and an approximate *S* value of 0.0035 can be calculated, corresponding to the product-forming reaction, on a per molecule basis, being about 280 times more likely with ethanol than with TFE.

Solvolysis of Benzyl Chloroformate (1): Kinetic Studies. The specific rates of solvolysis of **1** have been studied in a wide range of solvents including the highly ionizing and very weakly nucleophilic HFIP−H_2O mixtures. In contrast to the good overall correlation observed for solvolyses of **2**, application of the extended (two-term) Grunwald−Winstein equation (eq 1) to 26 solvolyses of **1** leads to a very poor correlation (correlation coefficient of 0.5324 and *F*-test value of only 4.5), with an *l* value of 0.39 ± 0.13, an *m* value of 0.26 ± 0.10, and a *c* value of −0.25 ± 0.46. The poor correlation and the very low *l* value suggest that, as with several other chloroformate,[4,5] chlorothioformate,[2,5] and chlorothionoformate esters,[3] there is a duality of mechanism, with the operation of an addition−elimination mechanism in highly nucleophilic and/or weakly ionizing solvents, and an ionization mechanism in weakly nucleophilic and/or highly ionizing solvents.

Good correlations are obtained when the 26 solvents are divided into two groups, with each group then analyzed using eq 1. An analysis of the specific rates of solvolysis in 11 solvents (consisting of the three HFIP−H_2O mixtures, TFE, the five TFE−H_2O mixtures, 90% TFE−10% EtOH, and 80% TFE−20% EtOH) leads to values of 0.25 ± 0.05 for *l*, 0.66 ± 0.06 for *m*, and −2.05 ± 0.11 for *c*. The very negative value for *c* is due to the experimental k_0 value relating to the alternative mech-

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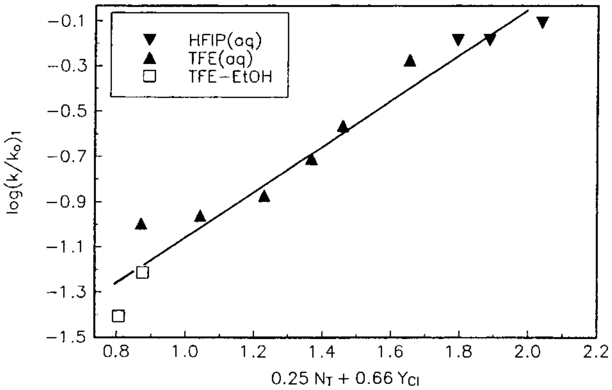

Figure 2. Plot of log(k/k_0) for solvolysis−decomposition of benzyl chloroformate in HFIP-H_2O, TFE, TFE−H_2O, 90% TFE−10% EtOH, and 80% TFE−20% EtOH against (0.25 N_T + 0.66 Y_{Cl}).

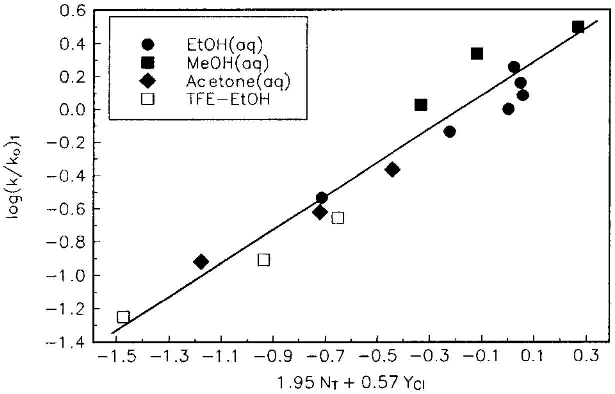

Figure 3. Plot of log(k/k_0) for solvolysis of benzyl chloroformate in the 15 solvents not included in Figure 2 against (1.95 N_T + 0.57 Y_{Cl}).

anism. The correlation coefficient of 0.9759 and the *F*-test value of 80 indicate an acceptable correlation (Figure 2).

For the other 15 solvents, values were obtained of 1.95 ± 0.16 for *l*, 0.57 ± 0.05 for *m*, and 0.16 ± 0.15 for *c*. The correlation coefficient of 0.9660 and *F*-test value of 83 again suggest an acceptable correlation (Figure 3). The *l*/*m* value of 3.42 ± 0.41 for the 15 solvents is essentially identical to the value of 3.50 ± 0.36 obtained for **2** in 19 solvents. Both the *l* and the *m* values are, however, higher (by 21% and 24%, respectively) than for **2**. This appears to be an anomaly resulting from the restricted set of solvents used in the analysis, unavoidable in the present case because of the change in mechanism. For the pathway considered to be addition−elimination, only three TFE−EtOH solvents of low TFE content represent the important fluoro alcohol-containing solvents. Consistent with this viewpoint, it can be shown that very similar *l* and *m* values are obtained when the solvolyses in 14 solvents, which are believed to operate by an identical addition−elimination mechanism for both **1** and **2**, are considered. For solvolyses of **1** the values are 1.95 ± 0.17 for *l* and 0.57 ± 0.05 for *m* (*l*/*m* value of 3.42 ± 0.42), and for solvolyses of **2** the values rise from those obtained in the wider range of solvents to values of 2.13 ± 0.16 for *l* and 0.60 ± 0.05 for *m* (*l*/*m* value of 3.55 ± 0.40).

In four solvents where the addition−elimination mechanism would be expected to operate, the values for the entropy of activation shown in Table 3 (in the range from −27 to −33 cal mol^{-1} K^{-1}) are consistent with a bimolecular rate-determining step. A value of −34 cal mol^{-1} K^{-1} was previously reported for ethanolyses.[21] For the ethanolysis, it was found that addition of 0.05 mol dm^{-3} tetraethylammonium chloride led to an increase in rate of 9.5% (Table 1). This could represent a modest salt effect but it could also be ascribed to a modest superimposed bimolecular attack at the benzylic carbon (attack at the carbonyl carbon would represent a symmetrical exchange reaction). A very pronounced bimolecular attack of this nature, equivalent to a chloride-ion catalyzed decomposition (eq 3), has been documented for several chloroformate esters in acetonitrile,[22] a dipolar aprotic

$$Cl^- + C_6H_5CH_2OCOCl \rightarrow C_6H_5CH_2Cl + CO_2 + Cl^- \quad (3)$$

solvent where the reduced solvation of the anion leads to considerably increased nucleophilicity.[23] Since the specific rates are in all cases calculated based on the experimental infinity titer, they are for the sum of solvolysis and decomposition.

Solvolysis of Benzyl Chloroformate (1): Product Studies. Consistent with the proposal that the mechanism with the low *l* value and the *l*/*m* ratio of 0.38 ± 0.08 represents an ionization mechanism, which by analogy with the reactions of 1-adamantyl chloroformate[7] might well involve a solvolysis−decomposition pathway, varying amounts of the benzyl chloride decomposition product are formed. The amounts of decomposition range from 1.3% in ethanol to 47.9% in TFE (Table 4). Also, varying amounts of benzyl ethyl ether from solvolyses in ethanol-containing solvents, and of benzyl 2,2,2-trifluoroethyl ether in TFE-containing solvents, were observed. The formation of these ethers requires the solvent capture to be associated with a loss of carbon dioxide.

Using the extended Grunwald−Winstein equation (eq 1) with incorporation of the values for the *l*, *m*, and *c* parameters reported above for the pathway believed to involve ionization, we can estimate a specific rate of ethanolysis by this mechanism of 4.24 × 10^{-8} s^{-1}, corresponding to about 0.1% of the overall ethanolysis rate (Table 1). Accordingly, only very small amounts of benzyl chloride and benzyl ethyl ether are predicted. The actual values of 1.3% and 0.6% (Table 4) are small, but higher than the prediction. This could, in part, be due to the long extrapolation in obtaining the estimated value, but it more probably results from the redevelopment of a small amount of benzyl chloride in the sample of **1** after its careful purification.

In solvents rich in fluoro alcohol, the products from the reactions of **1** under solvolytic conditions are largely those involving loss of carbon dioxide, with only small amounts of mixed carbonate ester (Table 4). For example, in TFE and 97% TFE, no benzyl 2,2,2-trifluoroethyl carbonate could be detected, and only 0.2% was formed from the reaction in 90% TFE. In 90% TFE−10% ethanol, only a trace (<0.1%) of this carbonate and only 1.9% of benzyl ethyl carbonate were detected. In these solvents, the amount of decomposition product ranged from 37% to 48%.

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In the preceding discussion, we have concentrated on products other than benzyl alcohol. This is because all reaction pathways involving nucleophilic attack by water (substitution at either benzylic or carbonyl carbon) ultimately lead to benzyl alcohol, due to the instability of alkyl hydrogen carbonates.[12,24,25]

In the presence of 0.02 and 0.05 mol dm^{-3} tetraethylammonium chloride, the amount of benzyl chloride formation accompanying the ethanolysis increased from 1.3% to 3.4% and 6.9%, respectively (Table 4). The 5.6% increase upon addition of the larger amount is close in value to the 7.6% increase in specific rate for this addition, suggesting that the increase in rate is largely due to a superimposed chloride-ion attack at the benzylic carbon of **1** (eq 3).

For reactions of **1** in aqueous ethanol, only minor amounts (0.6% in 90% ethanol to 1.9% in 50% ethanol) of benzyl ethyl ether are produced. If we assume that the selectivity ratios (S) of 1.7 to 4.4 previously reported for solvolyses of *p*-methoxybenzyl chloride in 90-50% aqueous ethanol[26] reflect capture of the *p*-methoxybenzyl cation and that these S values will also apply to a reasonable approximation to the capture of the parent benzyl cation, we can estimate that the amounts of benzyl alcohol produced by the solvolysis−decomposition (ionization) pathway will range, in terms of overall product formation, from 0.1% to 1.4%. These amounts represent a negligible contribution toward the experimental percentages of 14.9% to 42.0%. Accordingly, we can use the percentages of benzyl alcohol and benzyl ethyl carbonate to represent the products formed from attack of water or ethanol at the acyl carbon. The S values increase slightly with increasing water concentration and range from 2.0 to 4.1. The values of 2.7 and 3.7 for solvolyses in 80% and 60% ethanol can be compared with corresponding values for **2** of 4.1 and 6.1, indicating only a fairly small selectivity variation upon the introduction of the *p*-nitro substituent.

Surprisingly, the S values observed for the bimolecular attack at the acyl carbon of **1** by the addition−elimination pathway are, for solvolyses over the full range of ethanol−water compositions studied, essentially identical to those for the S_N2 solvolyses of benzyl chloride (or bromide) in these solvents at 75.0 °C. Values of 2.2, 2.5, 2.9, 3.1, and 3.3 were reported[27] for 90%, 80%, 70%, 60%, and 50% ethanol, respectively. The S value in 95% ethanol was essentially constant over a temperature range from 75−140 °C but the logarithm of the value in 50% ethanol varied as the inverse of the Kelvin temperature and extrapolation led to an S value of 4.3 at 25.0 °C, comparable to our value of 4.1 at this temperature.

In aqueous TFE solvents, the benzyl alcohol results primarily from the ionization−loss of carbon dioxide pathway. If we assume that the competing addition−elimination pathway has an S value similar to the 0.16 obtained for **2** in 80% TFE, we can estimate the percentages of overall reaction of the accompanying benzyl alcohol from the small amounts of benzyl 2,2,2-trifluoroethyl carbonate observed for reaction of **1** in 90−50% TFE. Those percentages are 0.6% in 90% TFE, 2.9% in 80% TFE, 7.7% in 70% TFE, and 21.2% in 50% TFE. These values are then deducted from the experimental percentages of benzyl alcohol prior to calculation, in the usual manner, of the S values for benzyl cation capture. A constant S value of 1.03 ± 0.02 is obtained over the range of 97−70% TFE, with the value increasing slightly to 1.20 at 50% TFE. These values can be compared to those obtained in this solvent composition range for *p*-methoxybenzyl chloride,[28] where the S value rises slightly with increased water content, from 0.36 in 97% TFE to 0.56 in 50% TFE. The lower values for *p*-methoxybenzyl chloride may result from the more stable carbocation showing a larger selectivity, favoring reaction with the more nucleophilic water. Another factor could possibly be that cations formed by loss of carbon dioxide from the chloroformate ester are more reactive and less selective, in a manner paralleling that well-documented for cations formed by nitrogen loss from diazonium ions.[29−31]

Table 6. Selectivity Values[a] for Reactions of Benzyl Chloroformate at 25.0 °C and Percentage of Overall Ionization Component Involving Decomposition to Benzyl Chloride

solvent[b]	S_{S-D}[c]	S_{Acyl}[d]	% Cl$^-$ capture[e]
90% EtOH		2.0	
80% EtOH		2.7	
70% EtOH		3.3	
60% EtOH		3.7	
50% EtOH		4.1	
97% TFE	1.05		46
90% TFE	1.01		37
80% TFE	1.02		29
70% TFE	1.04		23
50% TFE	1.20		15
90T-10E	0.81		45
80T-20E	0.83	0.0036	44
60T-40E	0.73	0.0066	49

[a] Defined as in eq 2; for TFE−ethanol (T−E) mixtures, for reaction with TFE relative to reaction with ethanol. [b] See footnote *a* to Table 4. [c] For the solvolysis−decomposition pathway (capture of the benzyl cation). [d] For attack at acyl carbon. [e] Relating only to the ionization reaction.

Maskill and Jencks[8a] determined the solvolysis products of the reaction of benzyl azoxytosylate ($C_6H_5CH_2$NONOTs) to be 76% the alcohol and 24% the ether, in a mixture of equal volumes of water and TFE (on a w/w basis 58.3% TFE) at 42 °C in the presence of 0.050 mol dm^{-3} sodium perchlorate, corresponding to an S value of 1.26. This value is in reasonable agreement with a value of 1.13 in the absence of added salt, obtained at 25.0 °C by interpolation within the data of Table 6. In contrast to the present study, where benzyl chloride formed by decomposition is essentially unreacted at 10 half-lives for the reaction of benzyl chloroformate,[11] benzyl tosylate solvolyzes in 1:1 (v/v) TFE−water[32] about 50 times faster, at a temperature 17 °C lower, than benzyl azoxytosylate, and it cannot accumulate during reaction. Reaction with benzyl tosylate as an intermediate probably involves product formation via an uncoupled

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S_N2 reaction, with bond breaking running ahead of bond making at the transition state.[32,33] Nonetheless, the *S* value of 0.94 with benzyl tosylate as the substrate[32] is very similar to the values obtained for benzyl azoxytosylate and benzyl chloroformate, such that if a portion of the reaction is via benzyl tosylate, it will not seriously perturb the comparison of *S* values. The similar *S* values for the azoxytosylate and the chloroformate are consistent with both pathways involving capture of an intermediate benzyl cation by the solvent.

In TFE−ethanol mixtures, we can measure the production of all four of the solvolysis products, two from attack at the acyl carbon and two from capture of the benzyl cation. This allows, in principle at least, the calculation of *S* values for both routes. In practice, in TFE-rich solvents only trace amounts of benzyl 2,2,2-trifluoroethyl carbonate are produced and in ethanol-rich solvents, only trace amounts of both benzyl 2,2,2-trifluoroethyl carbonate and ether.

The product percentages are reported in Table 4 and, for three of the mixtures, *S* values are reported in Table 6. Over the 90% to 60% (v/v) range of TFE content, the *S* value for benzyl cation capture is again very close to unity, as it was for the TFE−water mixtures. The value of 0.79 ± 0.05 shows only a slight preference for reaction with the more nucleophilic ethanol. This differs from the study of *p*-methoxybenzyl chloride in these solvents,[28] where the *S* values rose slightly with ethanol content and were much lower in value (0.040 to 0.068). To explain the surprising large difference between the partitioning between TFE and water and between TFE and ethanol, it was proposed[28] that TFE suppresses the nucleophilic attack by both water and ethanol, but with a larger effect for water. We do not see evidence for this large difference in our study. Our present results are, however, in accord with those for the solvolysis−decomposition of 1-adamantyl chloroformate, where an *S* value of 0.97 in 80% TFE and a range of *S* values from 1.64 to 1.13 in TFE−ethanol mixtures was observed.[7a]

The selectivity for reaction at the acyl carbon of 0.0036 in 80% TFE−20% ethanol (v/v) is essentially identical to the value of 0.0035 obtained for the reaction of **2** (Table 5), where 100% of the reaction follows this pathway, as opposed to 15% for **1**. In 60% TFE−40% ethanol (v/v), the *S* value increases to 0.0066. These small *S* values are consistent with the nucleophilic addition to the acyl carbon being rate-determining, with ethanol considerably more nucleophilic than TFE.

Conclusions

The solvolyses of *p*-nitrobenzyl chloroformate (**2**) give as products *p*-nitrobenzyl alcohol from reaction with the water component of a binary solvent and *p*-nitrobenzyl alkyl carbonate from reaction with an alcohol or with the alcohol component of a binary solvent. None of the product studies showed any formation of *p*-nitrobenzyl alkyl ether, strongly suggesting that the *p*-nitrobenzyl alcohol is formed in the decomposition of an intermediate *p*-nitrobenzyl hydrogen carbonate.

Multiple correlation analysis of the specific rates of solvolysis against a combination of solvent nucleophilicity (N_T) values and solvent ionizing power (Y_{Cl}) values leads to a sensitivity toward changes in solvent nucleophilicity (*l* value) of 1.61 ± 0.09 and a sensitivity toward changes in solvent ionizing power (*m* value) of 0.46 ± 0.04. These values are typical of those obtained when the association step within an association−dissociation (addition−elimination) mechanism is rate-determining. Five measured values for the entropy of activation, in the range −30 to −38 cal mol^{-1} K^{-1}, are consistent with this hypothesis.

The selectivity values (*S*) obtained in binary solvents are also consistent with the proposed mechanism. In 80% and 60% (v/v) ethanol, reaction with the more nucleophilic ethanol is preferred over reaction with water by factors of 4.1 and 6.1, respectively. In 80% TFE−20% ethanol (v/v), with a much greater difference in nucleophilicities, ethanol is favored over TFE by a factor of 286.

The solvolyses of benzyl chloroformate (**1**) can give, in addition to the alcohol and mixed carbonate esters, two additional types of product, formed with loss of CO_2: benzyl chloride (the decomposition product) and benzyl alkyl ethers. Formation of these additional types, relative to the products from **2**, are favored in solvents of low nucleophilicity and/or high ionizing power. In other solvents, the products are very similar in character and amount to those formed from **2**.

Multiple correlation analyses were carried out after division of the 26 available data points into two groups, based on solvent characteristics. For 11 solvents, comprising TFE, all of the TFE and HFIP mixtures with water, and the two TFE−ethanol mixtures of highest TFE content, *l* values of 0.25 ± 0.05 and *m* values of 0.66 ± 0.06 were obtained. These values are suggestive of an ionization mechanism, as similar rather low *m* values have previously been found to be a characteristic of ionization reactions proceeding with an accompanying loss of a small molecule. The other 15 solvents produce *l* and *m* values (1.95 ± 0.16 and 0.57 ± 0.05, respectively) which are very similar to those observed for solvolyses of **2**.

With the assumption that the products from the association−dissociation pathway for **1** will approximate the partitioning observed for **2**, thus allowing one to subdivide the total alcohol product into components from each pathway, one can calculate *S* values for each pathway. In aqueous ethanol (favoring the association−dissociation pathway), values of 2.7 and 3.7 are obtained in 80% and 60% ethanol (v/v). These values are slightly lower, but similar to, values obtained for solvolyses of **2**. In 80% TFE−20% ethanol, the *S* value of 278 for this pathway is essentially identical to that observed for **2**. In TFE−H_2O mixtures with 97−50% TFE (w/w), an essentially constant value, close to unity, is observed for reaction by the ionization pathway, which falls to only just below unity for TFE−ethanol mixtures. These very low selectivity values are consistent with the capture by the components of the solvent of a high-energy unselective carbocation. Values very close to unity are often observed when the products are formed at the solvent-separated ion-pair stage. A benzyl carbocation−chloride anion pair is formed, which can either collapse to decomposition product or allow solvent to insert and then react, leading to solvolysis products being formed after loss of CO_2.

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Experimental Section

Materials. Benzyl chloroformate (**1**, Aldrich) was separated from benzyl chloride impurity (from decomposition) by repeated fractional distillation at reduced pressure. In the ^1H NMR spectrum ($CDCl_3$), the signals due to the methylene protons of **1** (δ 5.3) and those of benzyl chloride (δ 4.5) are well separated. The reported specific rates and product studies were conducted using a purified sample, with no detectable signal at δ 4.5. The *p*-nitrobenzyl chloroformate (**2**, Aldrich) was recrystallized from petroleum ether and stored at 0 °C, mp 32−34 °C (lit.[10a] 33.5−34 °C). The solvents were purified and the kinetic runs carried out as previously described.[14]

Product Studies. The products from the reactions of **1** under solvolytic conditions were analyzed after 10 half-lives by gas chromatography (Shimazu GC-9A) using a 2.1 m glass column containing 10% Carbowax 20M on Chromosorb WAW 80/100. For the studies in most solvent mixtures, the column temperature was 130 °C but, due to similar retention times for the benzyl ethyl ether and benzyl 2,2,2-trifluoroethyl ether, it was reduced to 70 °C for the analyses of reactions in TFE−ethanol mixtures. Nitrogen was used as the carrier gas and a flame ionization detector was employed. The retention times (min) at 130 °C were as follows: BzOEt, 1.58; $BzOCH_2CF_3$, 1.63; BzCl, 2.03; $BzOCO_2CH_2CF_3$, 6.91; BzOH, 8.63; and $BzOCO_2$-Et, 12.37. At 70 °C, the corresponding values were 7.66, 8.82, 10.02, 27.02, 28.04, and 32.22.

The products from the solvolyses of **2** were analyzed by gas chromatography/mass spectroscopy (Fisons TRIO 1000), with nitrogen as carrier gas and with the same column conditions as those used for **1**.

In a control experiment to see the maximum possible extent of subsequent reaction of the benzyl chloride formed by decomposition, a 0.0050 M solution was allowed to react in 70% TFE (w/w) for 42 h at 25.0 °C, the time for 10 half-lives for reaction of **1** under these conditions. Only 3.0% of the benzyl chloride was converted to solvolysis product (2.5% benzyl alcohol and 0.5% benzyl 2,2,2-trifluoroethyl ether). After 113 h, there was 6.2% benzyl alcohol and 1.5% benzyl 2,2,2-trifluoroethyl ether formation.

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